## EXHIBIT B

## MARKED UP VERSION OF AMENDED SPECIFICATION AND CLAIMS

In the Specification

At page 30 line 16:

Studies by Aiura et al. [9Cytokine] (Cytokine 1991;4:498) have shown that Interleukin-1 receptor antagonist is protective in a rabbit model of hypotensive gram-positive septic shock. The administration of Interleukin-1 receptor antagonist in this animal model has been shown to maintain mean arterial pressure compared to control, as well as decreasing lung water and maintaining urine output. This work demonstrated the role of Interleukin-1 and the protective role of Interleukin-1 receptor antagonist in gram-positive septic shock. Interleukin-1 is the principal mediator in a patient's clinical response to multiple different stresses regardless of the etiology (including acute pancreatitis, sepsis, endotoxin shock, and cytokine induced shock).

At page 33 line 23:

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, Calif., U.S.A. (the [MaxBat.RTM] MAXBAT™ kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

At page 33 line 31:

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, [heparin-toyopearl.RTM]



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HEPARIN-TOYOPEARL™ or [Cibacrom blue 3GA Sepharose.RTM.] CIBACROM 3GA SEPHAROSE™; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

At page 42 line 29:

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I [ .alpha.] $\alpha$ chain protein and [.beta..sub.2] $\beta_2$ microglobulin protein or an MHC class II [.alpha.] $\alpha$ chain protein and an MHC class II [.beta.] $\beta$ chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

At page 50 line 16:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience

(Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28); Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

At page 101, line 19:

A plurality of novel nucleic acids were obtained from the FSK001 cDNA library (prepared from human fetal skin tissue mRNA purchased from Invitrogen, San Diego, CA) using standard PCR, SBH sequence signature analysis and Sanger sequencing techniques. The inserts of the library were amplified with PCR using primers specific for pSport1 (GIBCO BRL, Grand Island, N.Y) vector sequences which flank the inserts. These samples were spotted onto nylon membranes and interrogated with oligonucleotide probes to give sequence signatures. The clones were clustered into groups of similar or identical sequences, and single representative clones were selected from each group for gel sequencing. The 5' sequence of the amplified inserts was then deduced using the reverse M13 sequencing primer in a typical Sanger sequencing protocol. PCR products were purified and subjected to flourescent dye terminator cycle sequencing. Single pass gel sequencing was done using a 377 Applied Biosystems (ABI) sequencer. One cDNA insert was identified by sequencing of several hundred base pairs (approximately 1-386 of SEQ ID NO: 1) as a novel sequence related to IL-1Ra that had not been previously reported in public databases. The remaining sequence of SEQ ID NO: 1 was obtained by further sequencing of the entire cDNA insert of the same clone; the sequence was confirmed in part by sequencing of 5' RACE PCR products from fetal skin and adult brain cDNA libraries. This sequence and the clone were designated by code name CG149 and clone name RTA00003379F.h.20 (later redesignated pIL-1Hy2 and deposited at the ATCC on May 21, 1999 under Accession No. PTA-96), and the encoded polypeptide was designated IL-1Ra-Hy2 (later redesignated IL-1Hy2).

At page 105 line 6:

IL-1 Hy2 and fragments thereof that include a receptor binding region are useful as reagents to identify cells and tissues expressing IL-1 receptors. The IL-1 receptor binding assay described in Hannum et al. Nature 343:336-340 (1990) may be used. Briefly, highly radioactive recombinant SEQ ID NOS: 2 or 4 is prepared by

growing [E.coli] *E. coli* expressing either of SEQ ID NOS: 2 or 4 on M9 medium containing [[35S] sulphate] $^{35}$S-sulfate and purifying the labeled recombinant polypeptide by chromatography on a Mono-S column. The labeled polypeptide is incubated with the cells or tissue under standard IL-1 binding assay conditions, and [[35S]] $^{35}$S binding. Significant [[35S]] $^{35}$S binding indicates the presence of IL-1 receptors.

At page 108 line 14:

Murine D10 cells, an Interleukin-1 dependent T-cell line, are used to measure Interleukin-1 mitogenic activity. Cell proliferation in the present of Interleukin-1 with and without the IL-1 Hy2 polypeptides of the invention is assessed by incorporation of ([ sup 3]
$^{3}$H) thymidine as previously described (Bakouche, O., et al. J. Immunol. 138:4249-4255, 1987). In a preferred embodiment, antagonists and agonist of the IL-1 Hy2 polypeptides of the invention are identified in this assay by adding the candidate compounds with the Interleukin-1 and IL-1 Hy2 polypeptides of the invention and measuring the change in cell proliferation caused by the candidate compound.

At page 108 line 24:

Inhibition of Interleukin-1-induced cytotoxicity is studied using an appropriate cell line, such as, for example, A375 tumor cells plated at a density of 6000 cells per well in 96-well microliter plates. After overnight attachment, Interleukin-1 (3-300 ng/mL) is added in the presence or absence of NAA or NMA. After cells are incubated for 3 days, ( [sup 3]
$^{3}$H) thymidine is added (1 mu Ci per well) for an additional 2 hours. Cells are harvested onto glass fiber disks (PHD Cell Harvested; Cambridge Technology, Inc., Watertown, Ma.) Disks are air dried overnight, and radioactivity is determined with a Model 1900TR Scintillation Counter (Packard Instrument Division, Downers Grove, Ill.)

At page 109 line 2:

Aortic smooth muscle cells are cultured by explanting segments of the medial layer of aortas from adult male Fischer 344 rats. Aortas are removed aseptically and freed of adventitial and endothelial cells by scraping both the luminal and abluminal

surfaces. Medial fragments are allowed to attach to Primaria 25-[cm sup 2] $cm^2$ tissue culture flasks (Becton-Dickinson, Lincoln Park, N.J.) which are kept moist with growth medium until cells emerged. Cultures are fed twice weekly with medium 199 containing 10% fetal bovine serum, 25 mM HEPES buffer (pH 7.4), 2mM L-glutamine, 40 mu g/mL endothelial cell growth supplement (Biomedical Technologies, Inc., Stoughton, Mass.) and 10 mu g/ml gentamicin (GIBCO BRL, Grand Island, N.Y.). When primary cultures become confluent, they are passaged by trypsinization, and explants are discarded. For these studies, cells from passages 12-14 are seeded at 20,000 per well in 96-well plates and are used at confluence (60,000-80,000 cells per well). The cells exhibit the classic smooth muscle cell phenotype with hill and valley morphology, and they stain positively for smooth muscle actin.

At page 109 line 15:

Rat aortic smooth muscle cells are incubated with RPMI-1640 medium containing 10% bovine calf serum, 25 mM HEPES buffer (pH 7.4), 2 mM glutamine, 80 mu g/mL penicillin, 80 mu g/mL steptomycin, 2 mu g/mL fungizone, 30 mu g/mL lipopolysaccharide (Escherichia coli 0111:B4), and 50 U/mL [IFN-y] INF-γ. Cells are harvested after 24 hours, and cytosol is prepared (Gross, S. S., et al. Biochem. Biophys. Res. Commun. 178:823-829, 1991). Cytosolic NO synthase activity is assayed by the $Fe^{2+}$ [sup 2+] -myoglobin method described previously (Gross, S. S., et al. Biochem. Biophys. Res. Commun. 178:823-829, 1991).



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